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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte KEITH HENRY STOCKMAN CAMPBELL
and IAN WILMUT,
APPELLANTS

Appeal 2007-1617
Application 09/225,233[1]
Technology Center 1600

Decided: 30 January 2008

Before FRED E. McKELVEY, *Senior Administrative Patent Judge*, and SALLY G. LANE, and MARK NAGUMO, *Administrative Patent Judges*.

NAGUMO, *Administrative Patent Judge*.

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[1]Application filed 4 January 1999, claiming benefit under 35 U.S.C. §§ 120 and 371 via intermediate applications to 30 August 1996, and the benefit under 35 U.S.C. § 119(a) back to 31 August 1995. The real party in interest is listed as Roslin Institute (Edinburgh), of Great Britain; Start Licensing, Inc., Exeter Life Sciences, Inc., and Geron Corp. are listed as licensees. (Appeal Brief filed 16 June 2006 ("233 Br."), at 2.)

DECISION ON APPEAL

A. Introduction

In Appeal 2007-1617, Appellants ("Campbell") seek review under 35 U.S.C. § 134 of the final rejection of claims 146–163, all the pending claims in application 09/225,233 (the "233 application").

In related Appeal 2007-2989, Appellants ("Campbell") seek review under 35 U.S.C. § 134 of the final rejection of claims 152–171, all the pending claims in application 09/658,862[2] (the "862 application").

Oral argument was heard before a court reporter on 19 September 2007.[3]

We have jurisdiction under 35 U.S.C. § 6(b). We AFFIRM.

As discussed *infra*, the Examiner and Campbell have treated the two appeals essentially as a single appeal. Corresponding claims of the two applications have been rejected in view of the same art on the same statutory grounds. Campbell has responded with essentially the same arguments in both appeals. Moreover, with one exception, the subject matter of the claims in each of the two applications has not been distinguished from that of the

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[2] Application filed 8 September 2000, claiming benefit under 35 U.S.C. §§ 120 and 371 via intermediate applications to 30 August 1996, and the benefit under 35 U.S.C. § 119(a) back to 31 August 1995. The real party in interest is listed as Roslin Institute (Edinburgh), of Great Britain; Start Licensing, Inc., Exeter Life Sciences, Inc., and Geron Corp. are listed as licensees. (Appeal Brief filed 16 June 2006 ("862 Br.") at 2.)

[3] (Transcript of Oral Argument held 19 September 2007, ("Transcript").)

other by technical details of the processes recited in the claims. The sole exception is in the discussion of the mutual provisional double patenting rejections. Accordingly, we discuss the appeals together and enter Decisions that differ only in the Summary sections. Complete statements of the rejections of the claims of both applications are entered in each decision to facilitate comparison of the two appeals.

The subject matter on appeal relates to clones of mammals. A clone is a genetic copy of a living thing. Forms of life that can reproduce asexually — e.g., by fission or budding—naturally produce clones. More "advanced" forms of life tend to reproduce sexually, rather than asexually. Mammals, for example, are not known to reproduce naturally by cloning.

The general concept of cloning is now well-known from accounts in the popular press. The 233 application explains cloning in the following general terms: an embryo is "reconstructed" by transferring [*in vitro*] a nucleus from a donor embryo to an enucleated oocyte (an egg cell with its nucleus removed). Development then proceeds [*in vivo*, following implantation of the resulting reconstructed embryo into a host mother] to live offspring. (233 application at 1.) A problem with this approach, however, is that there are only 32 to 64 cells per embryo at the stage most widely used for the cloning of farm animals. (*Id.*) More plentiful sources of cells are said to be desirable, and cells that can be maintained in culture are said to be especially sought in the art. (*Id.*) Somatic cells (i.e., differentiated, non-germ line cells) are said to satisfy these requirements.

(*Id.* at 4, first paragraph.) To be useful for cloning, however, the nucleus of a somatic cell must be "reprogrammed" or "de-differentiated" so it can develop into all cell types of the mature animal. (*Id.* at 2, last paragraph.)

The 862 and the 233 applications provide slightly different approaches to solving this problem. The subject matter claimed in the 862 application is certain live-born mammals cloned from nuclei of non-embryonic (i.e., differentiated, or "somatic") cells. The 233 application adds the further requirement that the donated nuclei come from non-foetal cells, i.e., that the nuclei come from cells originating in a live-born individual. The general process is now known as "somatic cell nuclear transfer," or "SCNT" cloning. Because neither the Examiner nor Campbell has argued the technical details of either process, the presence of the non-foetal limitation in the 233 application and its absence in the 862 application suffice to distinguish the claims of the two applications for the present discussion.[4]

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[4] The 233 application teaches that any cell of normal karyotype (full complement of chromosomes), including fully differentiated cells, can be a donor of a nucleus for cloning provided the donor cell is in a quiescent state, usually labeled "G0," of the mitotic cell cycle. (233 specification at 7–8.) According to the claims of the 233 application, the recipient cell must be in a "suitable state," which in preferred embodiments is "an enucleated metaphase II oocyte, an enucleated unactivated oocyte or an enucleated preactivated oocyte." (233 application at 11.)

In contrast, the 862 application teaches that the donor nucleus must come from a cell in the G0 or G1 (both are diploid) phase of the cell cycle. (862 specification at 7-8.) The 862 claims specify that the nuclei must come from G1 phase cells—and that the enucleated oocyte must be arrested in a

The claims have been rejected along parallel lines in each application.[5] The same references have been applied as prior art against corresponding claims in each application. The same references have been applied as evidence of the state of the art as of the time of filing of each application. The substantive arguments for rejection are essentially identical in the two applications. Campbell has responded with substantially the same arguments in its briefs for the two applications.[6] The substantive arguments for reversal are essentially identical. At oral argument, counsel for Campbell agreed that there were no distinct arguments for patentability in one application as compared to the other application. (Transcript at 2:20-25). Accordingly, we enter a common Decision in each application.

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the "metaphase II" state of development. (*See* also, 862 application at 8–9.)

[5] In the 233 application, see the Examiner's Answer mailed 11 September 2006 ("233 Answer") and the Final Rejection mailed 17 August 2005, incorporated by reference in the Answer.

In the 862 application, see the Examiner's Answer mailed 12 September 2006 ("862 Answer") and the Final Rejection mailed 16 August 2005, incorporated by reference in the Answer. When reasonable, the Answers will be cited collectively as "Answers."

[6] In the 233 application, see the Appeal Brief filed 16 June 2006 ("233 Brief") and the Reply Brief filed 13 November 2006 ("233 Reply"); in the 862 application, see the Appeal Brief filed 16 June 2006 ("862 Brief") and the Reply Brief filed 13 November 2006 ("862 Reply"). For the most part, the texts of the Briefs and Replies are identical. Accordingly, when reasonable, the Briefs and Replies will be cited collectively as "Briefs" or "Replies."

The subject matter on appeal relates to animals—specifically cattle, sheep, pigs, goats, mice, rabbits, horses, and rats—that are the products of two different cloning processes.

In particular, all of the claims in each application stand rejected:

(1) for lack of statutory subject matter under 35 U.S.C. § 101;

(2) for provisional double patenting under 35 U.S.C. § 101 against the claims of the other application; and

(3) as anticipated or obvious ("hybrid" rejections[7]) in view of various prior art references describing cloned animals and in two cases ordinary animals.

Moreover, in each application, claims drawn to cloned mice, rabbits, horses and rats stand rejected for lack of an enabling disclosure under 35 U.S.C. § 112(1). The enablement of claims drawn only to cloned cattle, sheep, pigs, and goats has not been challenged.

The Claims

The independent claims of the two applications that do not expressly recite specific process steps read (emphasis added):

[7] "The court has accepted the PTO's practice of basing rejections on sections 102 or 103 in the alternative, provided that the appellant was fully apprised of all the grounds of rejection. *See, e.g., In re Pearson*, 494 F.2d 1399, 1402 & nn. 2-3 (CCPA 1974)." *In re Spada,* 911 F.2d 705, 707 n.2 (Fed. Cir. 1990).

09/225,233 Claim 155

A live-born clone of a pre-existing, non-embryonic, **non-foetal**, donor mammal,

wherein the mammal is selected from cattle, sheep, pigs, goats, mice, rabbits, horses, and rats.

(233 Brief Claims App. at 2.) Claims 156–163 depend from claim 155.

09/658,862 Claim 163

A live-born clone of a pre-existing, non-embryonic, donor mammal,

wherein the mammal is selected from cattle, sheep, pigs, goats, mice, rabbits, horses, and rats.

(862 Brief Claims App. at 2.) Claims 164–171 depend from claim 163.

The independent product-by-process claims of each application are presented below in parallel on separate pages to facilitate comparison.

09/225,233 Claim 146:

A live-born clone of a pre-existing, non-embryonic, **non-foetal,** donor mammal

from which a differentiated cell has been taken,

wherein the mammal is selected from cattle, sheep, pigs, goats, mice, rabbits, horses, and rats,

wherein the clone is produced by a process comprising:

(a) transferring the nucleus of

a somatic cell of the non-embryonic, non-foetal, mammal

or a cell obtained by culture thereof

into a
suitable enucleated recipient cell from the same species,

wherein the **somatic** cell or cell obtained by culture thereof is a **quiescent diploid cell**

at the time of transfer;

(b) activating the **recipient cell** **before, during, or after nuclear transfer**;

(c) incubating the **reconstituted cell** such that an embryo develops;

(d) transferring the embryo to a female of the same species; and

(e) developing the embryo into the live-born clone.

(233 Brief Claims App. at 1; emphasis added.)

Claims 147–154 of the 233 application depend from claim 146.

09/658,862 Claim 152:

A live-born clone of a pre-existing, non-embryonic, donor mammal

from which a differentiated cell has been taken,

wherein the mammal is selected from cattle, sheep, pigs, goats, mice, rabbits, horses, and rats,

wherein the clone is produced by a process comprising:

(a) transferring the nucleus of

the differentiated cell

or a cell obtained by culture thereof

into an

enucleated, metaphase II-arrested oocyte from the same species,

wherein the **differentiated cell** or cell obtained by culture thereof is a **diploid cell in the G1 phase of the cell cycle**

at the time of transfer;

(b) activating the **oocyte**; and

(c) incubating the **activated oocyte** such that an embryo develops;

(d) transferring the embryo to a female of the same species; and

(e) developing the embryo into the live-born clone.

(862 Brief Claims App. at 1; emphasis added.)

Claims 153–162 of the 862 application depend from claim 152.

B. The Rejections: Findings of Fact and Discussion

Generally, neither Campbell nor the Examiner dispute facts found by the other. Rather, it is the inferences and conclusions drawn from those facts that are in dispute. The findings of fact set out in this Decision are supported by a preponderance of the evidence of record.

On appeal, the procedural burden is on the applicant to demonstrate error in the examiner's rejections. Arguments not raised in the principal brief on appeal are waived. 37 C.F.R. § 41.37(c)(1)(vii).

Nonstatutory Subject Matter

Nonstatutory subject matter is defined by 35 U.S.C. § 101, which reads:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

The predecessor to our reviewing court held that "[t]he word 'new' in § 101 is defined and is to be construed in accordance with the provisions of § 102. Thus, that which possesses statutory novelty under the provisions of § 102 is also new within the intendment of § 101. We have found no evidence of Congressional intent to define the word 'new' as used in § 101 in any different manner." *In re Bergstrom*, 427 F.2d 1394, 1401 (CCPA 1970) (footnote omitted).

Campbell relies on the testimony of Dr. David Wells for support of its arguments regarding technical aspects of cloning. (Briefs at 22.) Dr. Wells testifies that he earned a Ph.D. from the University of Edinburgh in 1991,

and that he gained competence in embryonic stem cell isolation working in the laboratory of Dr. Ian Wilmut, one of the inventors for Campbell. (Wells Declaration at 2, ¶ 3.) We find Dr. Wells well-qualified to explain matters in this area of technology.

In particular, Dr. Wells explained that a cloned mammal can be distinguished from an ordinary animal:

> Based on my experience with mammals cloned by nuclear transfer and mammals propagated by sexual reproduction, the source of a mammal's chromosomes can be readily determined using genetic analysis. By using genetic analysis, whether a mammal is cloned asexually by somatic cell nuclear transfer or propagated by sexual reproduction, including a mammal produced by nuclear transfer from an embryonic cell, can be determined by comparing the chromosomal DNA of the mammal to that of its parent(s). Only a mammal cloned by somatic cell nuclear transfer will contain the same set of chromosomes as a single parental mammal.

(Wells Declaration at 8, ¶ 33.)

Dr. Wells explained the differences between a cloned mammal and a mammal produced by sexual reproduction in the following words:

> Based on my experience with mammals cloned by nuclear transfer and mammals propagated by sexual reproduction, a mammal cloned by somatic cell nuclear transfer is unlike any mammal produced by a process involving sexual reproduction, including a mammal produced by nuclear transfer from an embryonic cell. The set of chromosomes of a mammal cloned by somatic cell nuclear transfer is obtained from a single parental mammal. The set of chromosomes from any mammal produced by a process involving sexual reproduction, including a mammal produced by nuclear transfer from an embryonic cell, comes from two parental mammals, one male and one female. This feature allows the cloned mammal to preserve the genetic information of the parental mammal without dilution.

(Wells Declaration at 8, ¶ 34.)

Dr. Wells also explained how a cloned mammal could be distinguished from the donor mammal:

> Based on my experience with cloned mammals, a mammal that contains the same set of chromosomes as a single parental mammal can be distinguished from the parental mammal due to environmental influences. First, the cloned mammal will always be of a younger age than the parental mammal. Second, the cloned mammal will have a variety of phenotypic differences from the parental mammal, for example, differences in fur and skin pigmentation. Third, the cloned mammal will have behavioral differences from the parental mammal.

(Wells Declaration at 9, ¶ 35.)

The Examiner has rejected claims 146–163 of the 233 application and claims 152-171 of the 862 application under 35 U.S.C. § 101 as being drawn to non-statutory subject matter. The Examiner finds that the claimed mammalian clones are not sufficiently distinguished over pre-existing mammals of the same species. (Answer at 6.) In the Examiner's words, "[t]he method of making the mammals [i.e., cloning] does not imbue any new or novel characteristic to the cloned mammals, nor does the method imbue a new use to the mammals claimed. . . . The only discernable difference between the clone and the cattle . . . known in the art at the time of filing is how they were made." (*Id.*)

Campbell responds that the claimed cloned mammals are never found in nature because the cloned mammal has the identical nuclear genome as the donor mammal, whereas all naturally produced mammals have half the chromosomal complement of one parent and half the chromosomal complement of the other parent. (Brief at 6–8.) Campbell argues that

because the cloned mammals are the result only of human intervention, they are not naturally occurring products and are thus patentable subject matter. (Brief at 9–10.) Moreover, Campbell notes that, "[a]lthough appellants' claimed mammals are copies of a pre-existing, parental mammal, they are not the same mammal. They have phenotypic differences, occupy a different space, and exist during a different time than the parental mammal." (Briefs at 4, citations to the respective specifications omitted.)

Responding to Campbell's arguments, the Examiner urges that "[i]f the clones are the same as what appellant would agree is a product of nature [i.e., the pre-existing mammal], a mammal produced by sexual reproduction, then the mammals produced by nuclear transfer must also be products of nature. While there is evidence of the hand of man in methods of nuclear transfer, there is no evidence of the hand of man in the presently claimed live-born clones." (Answer at 18.)

At oral argument, the merits panel asked how the claimed clones differ from identical twins, which have the same set of chromosomes as one another. Campbell responded that "[i]t gets down to the age difference. Identical twins are always the same age." (Transcript at 5:26–27.) In contrast, Campbell argued, "nature does not make a clone of something that preexisted it. It simply doesn't exist in nature so you have that age difference." (*Id.* at 6:8–9.)

We are confronted with what appears to be a case of first impression —a challenge to the status of a cloned mammal as patentable subject matter. The clones are very close copies of a pre-existing animal. The closer the

copy, the more successful the cloning procedure. Can it be that a copy of a preexisting thing is patentable subject matter?

Initially, we find that mammals do not naturally reproduce by cloning or budding. Thus, the argument is very strong that a cloned mammal covered by the present claims is, in the words of the Court, "a nonnaturally occurring manufacture or composition of matter—a product of human ingenuity." *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980). In that case, the Court found that Chakrabarty's claim was "not to a hitherto unknown natural phenomenon, but to a nonnaturally occurring manufacture or composition of matter-a product of human ingenuity 'having a distinctive name, character [and] use.'" *Id.* at 309–10, *quoting Hartranft v. Wiegmann*, 121 U.S. 609, 615 (1887).

Nonetheless, the term "new" in § 101 cannot be ignored, as all words of a statute must be given effect. We must therefore ask, what limitations of the claims distinguish the claimed product (a clone of a specified mammal) from other mammals of that type—in particular, from the donor of the nucleus? In answering this question, we must bear in mind that, as discussed in more detail in the next section, product-by-process claims are claims to the product itself, and are anticipated by the prior description of any product, no matter how made, that is the same as, or substantially the same as, a product made by the recited process.

The closest possible copy appears to be obtained by transferring[8] the nucleus of a somatic cell into an enucleated oocyte obtained from the same mammal and then implanting the resulting embryo into the uterus of the donor of the nucleus[9]. Assuming the components are negligibly perturbed by the procedure, the resulting clone would have the same nuclear and mitochondrial DNA and the same initial cytoplasm as the donor animal. The clone would develop in an environment governed by its own DNA. It appears that even a clone made by this procedure will not be an exact copy of the "parent," much as one identical twin is not identical to its twin. During the course of development, which genes are turned on and off at what time and to what extent and to what effect will differ due to "environmental factors," resulting in physical differences. The claims also encompass clones in which the nuclear donor is a different individual than the oocyte donor, which is a different individual from the surrogate mother. The latter appears to be the ordinary course. These latter clones will differ from the nuclear donor in many additional ways.

Differences, however, are patentably significant only to the extent that the different subject matter is encompassed by or excluded from the scope of the claimed subject matter. The Examiner found that a clone is not imbued with any new or novel characteristic compared to the parent as a result of the cloning procedure. Hence, the Examiner concluded, the clone is not "new"

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[8] According to Campbell, nuclear transfer is preferably accomplished by fusion of the donor cell with the enucleated oocyte. (*E.g.*, 233 specification at 12:30–33; 862 specification at 2:18–22.) Other methods of transfer, such as microinjection of the nucleus into the oocyte are also possible. (233 specification at 13:31–35; 862 specification at 10:18–21.)

[9] The foal reported by Galli, discussed *infra*, appears to be such a clone.

and patentable within the meaning of § 101. The Examiner's error, to the extent it was error, was to compare the individual cloned sheep to the set of all sheep, rather than to the specific donor of the nucleus. Focusing on the individual creatures emphasizes that a specific "copy" of an individual creature—as close a copy as technology and nature will allow—has been made.

The differences cited by Campbell—that the clones occupy a different space and exist during a different time than the parental animal—are trivial and are true of any two objects, one of which is a copy of the other. The phenotypic differences broadly cited by Campbell and by Dr. Wells are similarly trivial in that any pair of creatures as complicated as mammals will look and behave somewhat differently. Indeed, any two macroscopic objects will, in practice, not be completely identical on some scale. Such trivial and uncontrollable distinctions cannot be the basis of differences that result in patentable distinctness. Unlike a genetically altered life-form, the claimed mammal clones perform their original functions in their natural way. We find, in parallel with the Examiner, that the preponderance of the evidence indicates that the claimed cloned mammals do not differ in any substantive way from the nuclear donor parent. Indeed, Dr. Wells testifies that the clone is chromosomally identical to the parental animal. (Wells Declaration at 8, ¶¶ 33, 34.) Campbell has not shown, for example, that any phenotypic differences are a systematic result of the recited cloning processes. Rather, the differences appear to arise at random, beyond the control of the person doing the cloning. Although more complex, the differences are more like defects in a crystal than deliberate modifications. Because the recited processes do not result in products (cloned mammals)

having properties that distinguish them from the nuclear donors in a nontrivial way, we conclude that the claimed clones are not "new" within the meaning of § 101. In the words of the Court, the claimed cloned sheep, etc., do not have "markedly different characteristics from any found in nature." *Chakrabarty*, 447 U.S. at 310.

We conclude that claims of the present scope, drawn to clones of the recited mammals, are not drawn to statutory subject matter within the meaning of 35 U.S.C. § 101 because they are not "new" within the meaning of 35 U.S.C. § 102. It is not apparent to us what limitation in the rejected claims distinguishes—in the anticipation sense—the clone from the donor. Campbell has not shown reversible error in the Examiner's conclusion. Accordingly, the Examiner's rejections of all the claims in each application are AFFIRMED.

Because our reasoning differs from that of the Examiner, we enter this affirmance as a NEW GROUND OF REJECTION in order to afford Campbell a full and fair opportunity to respond. Should Campbell wish to respond solely on the basis of the present record, but feel that further oral argument would be helpful to present its case, we invite Campbell to submit, along with its response, a separate request for oral argument.

We consider the remaining rejections *in the alternative* to the threshold issue of patentable subject matter.

Provisional Statutory Double Patenting

The Examiner has provisionally rejected claims 146–163 of the 233 application over claims 152–171 of the 862 application, and vice-versa, under 35 U.S.C. § 101. The Examiner found that, although the recited

processes of nuclear transfer (i.e., of cloning) differ, the particular methods do not affect the structure, function, or the use of the claimed nonhuman mammals. (Answers at 4-5.) Accordingly, the Examiner concluded that the same mammalian clones are claimed in each application. (*Id.*)

Campbell argues that the same subject matter is not claimed because the claims of the 233 application include the limitation that the clone is of a pre-existing non-foetal donor mammal, whereas the claims of the 862 application do not contain this limitation. (Briefs at 5–6.) Campbell does not otherwise explain why mammals cloned from foetal mammals by the 862 process differ from the mammals cloned from non-foetal mammals cloned by the 233 process. In the Replies, Campbell argues that the complete mutual infringement test set out in *In re Vogel*, 422 F.2d 438, 441 (CCPA 1970), demonstrates that the claims of the two applications are not drawn to identically the same invention. (Replies at 2.)

The court, writing in *Vogel*, phrased the question this way: "Is the same invention being claimed twice? . . . 'invention' here means what is defined by the claims . . . By 'same invention,' we mean identical subject matter." 422 F.2d at 441. In this context, the court tested whether claims to a process of prolonging the storage life of packaged meat products were properly rejected under "same invention" type double patenting over claims to methods of processing pork by asking, "whether one of the claims could be literally infringed without literally infringing the other. If it could be, the claims do not define identically the same invention." (*Id.*) According to the court, this was "[a] good test, and probably the only objective test, for 'same invention.' (*Id.*)

As the development of the law of claim construction since *Vogel* has made clear, claims in an application are not analyzed in the same manner as claims in a patent. Our reviewing court explained:

> [d]uring patent examination the pending claims must be interpreted as broadly as their terms reasonably allow. . . . The reason is simply that during patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language explored, and clarification imposed. . . . An essential purpose of patent examination is to fashion claims that are precise, clear, correct, and unambiguous. Only in this way can uncertainties of claim scope be removed, as much as possible, during the administrative process.

In re Zletz, 893 F.2d 319, 321-22 (Fed. Cir. 1989). Hence, the court was wise to include the adverb "probably" in its characterization of its proposed test for double patenting. Although the "complete mutual infringement test" provides a useful analytical framework, it is important to keep in mind whether patent claims or—as here—application claims are being compared.

The difference between the construction of application claims and patent claims is particularly large for product-by-process claims. The Federal Circuit recently affirmed that, "[r]egardless of how broadly or narrowly one construes a product-by-process claim, it is clear that such claims are always to a product, not a process." *SmithKline Beecham Corp. v. Apotex Corp.*, 439 F.3d 1312, 1317 (Fed. Cir. 2006). The court pointed out that it has long been the law that "[i]f the product in a product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." (*Id.*, *quoting In re Thorpe*, 777 F.2d 695, 697 (Fed. Cir. 1985); *see also Atlantic Thermoplastics*, 970 F.2d 834, 847 (Fed. Cir. 1992) (endorsing the *Thorpe* analysis of application claims). Moreover, "[w]here . . . the

claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product." *In re Best*, 562 F.2d 1252, 1255 (CCPA 1977) (citation omitted). Thus, certainty of identity is not required to establish a prima facie case of anticipation or obviousness. Once a prima facie case of identical subject matter is established, the burden shifts to the applicant to come forward with evidence and argument in rebuttal. *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992).

On the present record, the claims of both the 233- and the 862-applications are drawn to clones of the same specified mammals, wherein the differences appear to lie, if at all, only in the source of the donor nuclei and in the detains of the recited process of somatic nuclear transfer. We find that Campbell's sole argument is based on the different scope of the donor of the nucleus: namely, that because the 862 application claims encompass mammals cloned from foetal cells, whereas the 233 application claims do not, the same subject matter is not claimed. As against application claims, this argument fails because it is incomplete. Campbell has not argued that a mammal cloned from foetal cell differs in any substantive way from a mammal of the same species cloned from a more developed cell. Nor has Campbell convincingly told us what limitation in the claims of one application distinguishes the product claimed in that application from the product claimed in the other application. We conclude that Campbell has failed to show that the Examiner's rejection for double patenting under 35 U.S.C. § 101 is in error.

Accordingly, we AFFIRM the rejection of claims 146–163 of the 233 application over claims 152–171 of the 862 application.

We also AFFIRM the rejection of claims 152–171 of the 862 application over claims 146–163 of the 233 application for provisional double patenting under 35 U.S.C. § 101.

Prior Art

The rejections over prior art fall into two classes. In Class 1, certain claims on appeal are rejected over prior reports of cloned animals obtained by admittedly different procedures. In Class 2, certain claims on appeal are rejected over prior reports of sexually reproduced mammals. In each case, the Examiner entered "hybrid" rejections under 35 U.S.C. §§ 102 or 103, as approved by the Federal circuit in *In re Spada*, 911 F.2d 705, 707–08 and 707 n.2 and n.3 (Fed. Cir. 1990).

A summary of the rejections follows.

Class 1

Ia. Claims 146, 147, 155, and 156 of the 233 application, drawn to clones of cattle, have been rejected under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Sims[10].

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[10]Michelle Sims and N.L. First, *Production of Calves by Transfer of Nuclei from Cultured Inner Cell Mass Cells*, 91 Proc. Nat'l. Acad. Sci. USA 6143-6147 (1994). The citation in the record, **90** Proc. Nat'l Acad. Sci. USA 6143 (**1993**) (emphasis added) is erroneous due to typographical errors in the heading of the document of record. A corrected copy of the article, obtained from the National Academy of Sciences website,

http://www.pnas.org/cgi/reprint/91/13/6143

has been made of record and a copy mailed to Applicants with this decision.

Ib. Claims 152–155, 163, and 164 of the 862 application, drawn to clones of cattle, have been rejected under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Sims.

IIa. Claims 146, 148, 155, and 157 of the 233 application, drawn to clones of sheep, have been rejected under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of McLaughlin[11].

IIb. Claims 152–154, 156, 163, and 165 of the 862 application, drawn to clones of sheep, have been rejected under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of McLaughlin.

IIIa. Claims 146, 149, 155, and 158 of the 233 application, drawn to clones of pigs, have been rejected under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Prather[12].

IIIb. Claims 152–154, 157, 163, and 166 of the 862 application, drawn to clones of pigs, have been rejected under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Prather.

IVa. Claims 146, 150, 155, and 159 of the 233 application, drawn to clones of goats, have been rejected under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Yong[13].

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[11]K.J. McLaughlin *et al.*, *In vitro Embryo Culture in the Production of Identical Merino Lambs by Nuclear Transplantation*, 2 *Reprod. Fertil. Dev.* 619-622 (1990).

[12]Randall S. Prather *et al.*, *Nuclear Transplantation in Early Pig Embryos*, 41 *Biol. Reprod.* 414-418 (1989). Michelle Sims and Neal L. First, the authors of art relied on in rejection I, are the co-authors.

[13]Z. Yong *et al.*, *Nuclear Transplantation in Goats*, 35 *Theriogenology* 299 (1991).

IVb. Claims 152–154, 158, 163, and 167 of the 862 application, drawn to clones of goats, have been rejected under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Yong.

Va. Claims 146, 151, 155, and 160 of the 233 application, drawn to clones of mice, have been rejected under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Cheong[14].

Vb. Claims 152–154, 159, 163, and 168 of the 862 application, drawn to clones of mice, have been rejected under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Cheong.

VIa. Claims 146, 152, 155, and 161 of the 233 application, drawn to clones of rabbits, have been rejected under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Yang[15].

VIb. Claims 152–154, 160, 163, and 169 of the 862 application, drawn to clones of rabbits, have been rejected under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Yang.

Class 2

VIIa. Claims 146, 153, 155, and 162 of the 233 application, drawn to clones of horses, have been rejected under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Lawrence[16].

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[14]Hee-Tae Cheong *et al.*, *Birth of Mice after Transplantation of Early Cell-Cycle-Stage Embryonic Nuclei into Enucleated Oocytes*, 48 *Biol. Reprod.* 958–963 (1993).

[15]Xiangzhong Yang *et al.*, *Nuclear Totipotency of Cultured Rabbit Morulae to Support Full-Term Development Following Nuclear Transfer*, 47 *Biol. Reprod.* 636–643 (1992).

VIIb. Claims 152–154, 161, 163, and 170 of the 862 application, drawn to clones of horses, have been rejected under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Lawrence.

VIIIa. Claims 146, 154, 155, and 163 of the 233 application, drawn to clones of rats, have been rejected under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Gonzales-Pacheco[17].

VIIIb. Claims 152–154, 162, 163, and 171 of the 862 application, drawn to clones of rats, have been rejected under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Gonzales-Pacheco.

The rejections of Class 1 rely on prior art disclosures of live-born clones made by transplanting an embryonic donor nucleus into an oocyte. The Class 1 reference processes differ from the processes recited in the application claims in that the application claims specify that a non-embryonic, non-foetal nucleus is transferred, (233 Application), or that a non-embryonic nucleus is transferred (862 Application). The rejections of Class 2 rely on prior art disclosures of sexually reproduced horses (VII: Lawrence) and rats (VIII: Gonzales-Pacheco).

In both classes of rejection, the Examiner found that the references describe live born clones and sexually reproduced offspring of the specific mammals, respectively. The Examiner found further that the live born clones and sexually reproduced offspring do not exhibit any novel structural or functional differences from those described in the reference. Following

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[16]Laurie Lawrence *et al.*, *Feeding Status Affects Glucose Metabolism in Exercising Horses*, 123 J. *Nutrition* 2152-2157 (1993).

[17]Diana M. Gonzales-Pacheco, *et al.*, *Energy Restriction Reduces Metabolic Rate in Adult Male Fisher-344 Rats*, 123 *J. Nutrition* 90-97 (1993).

cases such as *In re Best* and *Spada*, cited *supra*, the Examiner concluded that the claimed subject matter is anticipated, and that the burden fell on Campbell to show how it is not. In the alternative, the Examiner determined that, in the absence of structural or functional differences between the claimed mammals and the reference mammals, the claimed subject matter would have been obvious. (Answers at 9–15.)

Campbell argues all the rejections of all of the mammals together under separate headings of 102(b) (Briefs at 20–23) and 103(a) (Briefs at 23–25). Campbell does not make a different argument with respect to the 233 claims or the 862 claims.

With regard to anticipation, Campbell urges that the Examiner argues that, "since appellants' clone is a copy of what previously existed, appellants' clone is anticipated by its parental donor mammal." (Briefs at 20.) This, according to Campbell, is reversible error because "the prior art does not disclose animals that have all of the properties of appellants' claimed clones." (*Id.*) More particularly, Campbell argues that although the claimed clones have the same nucleus as the parent, the clones are not identical to the parent because they are derived from a different oocyte. (*Id.* at 21; Tr. at 10:8–10.) Campbell relies on the testimony of Dr. Wells, who stated that the cloned mammals described by each of the references relied on by the Examiner as evidence of anticipation or obviousness "do not contain the same set of chromosomes as either of their parents," (Wells Declaration ¶¶ 7, 11, 15, 19, 23, 27, and 31) and that "[d]ifferences and identities in chromosomes could be readily determined, for example, using the well-known technique of genetic analysis" (*id.* at ¶¶ 8, 12, 16, 20, 24, 28, and 32).

Moreover, according to Campbell, differences between the parent and the clone would arise from chromosomal rearrangements, mitochondrial DNA, and environmental factors (e.g., the uterine environment). (*Id.* at 22, citing prior art and Dr. Wells's declaration.) Finally, Campbell argues that because the claimed mammals must be clones of a pre-existing mammal, the clone is "always younger" than the parent, and therefore not identical. Because the clones would not be identical to the parents, Campbell urges, the parents cannot anticipate the clones. (*Id.*)

With regard to what Campbell regards as the obviousness prong of the Examiner's rejection, Campbell argues that the Examiner erred in maintaining that, because the claimed clone "is a copy of what previously existed, appellants' clone is not different from its parent in a way that provides a patentable distinction." (Briefs at 23.) Again, Campbell points to alleged differences between the claims clones and pre-existing mammals, including their status as "time-delayed copies," their distinction as having a complete set of chromosomes from a single parent, rather than from two parents, and various genetic and phenotypic differences that arise in the course of development that "are unknown until the clone is born." (*Id.* at 24.) These differences, Campbell argues, are nonobvious because prior to its invention, no somatic transfer mammalian clones existed; nor were they thought to be possible. (*Id.* at 25.)

With regard to the rejections of the claims of Class 1. Campbell does not dispute the Examiner's finding that the references describe cloned cattle, sheep, pigs, goats, mice, and rabbits. Nor does Campbell direct our attention to any evidence or argument of record that the clones produced by the processes recited in the appealed claims differ from clones produced by the

processes described in the references. Indeed, all of the properties identified by Campbell as being unique to its cloned mammals appear to be fully met by the reference clones. Thus, the reference clones have an identical chromosome set as the single nuclear donor. Moreover, to the extent that the donor of the oocyte was not the same individual as the nuclear donor, the reference clones differ from the nuclear donor in the same general ways as do Campbell's clones, including the trivial and patentably insubstantial "difference" that the clone is a "time-delayed copy."

The Federal Circuit, ruling on the anticipation of a patented product-by-process claim, explained: "[i]t has long been established that one cannot avoid anticipation by an earlier product disclosure by claiming the same product more narrowly, that is, by claiming the product as produced by a particular process." *SmithKline*, 439 F.3d at 1317. In the present case, Campbell has failed to carry its burden on appeal, and has not come forward with evidence showing that the products claimed—the cloned mammals—are identifiably distinct from the mammals previously cloned, albeit by other techniques.

We therefore AFFIRM the Examiner's rejection of the cloned cattle, sheep, pigs, goats, mice, and rabbits over the corresponding prior art clones.

Campbell's arguments have weight against the rejections in Class 2, over Lawrence (sexually reproduced foal) and Gonzales-Pacheco (sexually reproduced laboratory rat) to the extent we give weight to the identity of the nuclear genome of the clone and that of the nuclear donor.[18] A comparison

[18] *See* the 862 Specification at 2:1–5 (explaining that the absence of chromosomal rearrangement and varying cytoplasmic contributions would have to be established to ensure that clones, "[i]n the true sense of the

of the chromosomal DNA of the claimed clones with that of the donor would be expected to show virtual identity. In contrast, a comparison of the DNA of sexually reproduced horses and rats of the references with that of either one of the parents would be expected to show only 50% identity. The Examiner has not relied on evidence that a horse or rat having the same nuclear genetic code as a previously existing horse or rat existed or was enabled prior to Campbell's disclosure.

The critical question raised by these two rejections is, "does the identity of the nuclear genetic code make a patentable difference?" The Examiner argues that it does not, because the cloned horse or rat is functionally like any other horse or rat. No specifically designed genetic alteration exists in the clones. On the present record, the only thing that makes the clones different from other horses or rats is that their nuclear genetic code is the same as another, older, horse or rat. It is true that each horse or rat clone is an individual being, distinguishable in theory from all other horses or rats. But absolute distinguishability is not a bar to anticipation or obviousness.

Weighing the evidence and arguments on both sides, we conclude that Campbell has identified a property of the clones that is enabled and that arises out of the recited processes of making. (Claims 155–163 of the 233 application and claims 163–171 of the 862 application are product-by-process claims, in that the products can only be made by cloning the

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meaning," had been made. It does not appear on this record that Campbell or the art tend to use the term "clone" in the "true sense of the meaning," which we understand to be an exact copy.

"parent.") The Examiner's rejection does not rely on art illustrating this property.

As Campbell has demonstrated that the Examiner's fact-finding is erroneous, we REVERSE the Examiner's rejections of the claims of Class 2, namely claims 146, 153–155, 162, and 163 of the 233 application, and claims 152-154, 161–163, 170, and 171 of the 862 application, all of which are drawn to cloned horses or to cloned rats.

Enablement

The enablement prong of 35 U.S.C. § 112(1) requires that the disclosure enable "any person skilled in the art to which [the claimed invention] pertains, or to which it is most nearly connected, to make and use" it. Our reviewing court has explained that:

> routine experimentation does not constitute undue experimentation: The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention.

Johns Hopkins Univ. v. CellPro, Inc., 152 F.3d 1342, 1360 (Fed. Cir. 1998). Whether the amount of experimentation necessary is undue is a legal conclusion based on underlying facts such as those set out in *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). Among the factors that may be considered are the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and

the breadth of the claims. *Id.* at 737. The so-called Wands factors are neither mandatory nor complete: which factors are important depend on the facts of each case. *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1371 (Fed. Cir. 1999) (citation omitted).

In the present case, the Examiner has maintained rejections for lack of enablement of claims covering live-born clones of rabbits, mice, rats, and horses. (Answers at 6–9.)

In the 233 application, claims 146, 151–155, and 160-163 have been rejected for lack of an enabling disclosure.

In the 862 application, claims 152–154, 159–163, and 168–171 have been rejected for lack of an enabling disclosure.

The rejected claims, broken down expressly by species, are:

IXa. Live-born rabbit clones: claims 146, 152, 155, and 161 of the 233 application.

IXb. Live-born rabbit clones: claims 152–154, 160, 163, and 169 of the 862 application.

Xa. Live-born mouse clones: claims 146, 151, 155, and 160 of the 233 application.

Xb. Live-born mouse clones: claims 152–154, 159, 163, and 168 of the 862 application.

XIa. Live-born rat clones: claims 146, 154, 155, and 163 of the 233 application.

XIb. Live-born rat clones: claims 152–154, 162, 163, and 171 of the 862 application.

XIIa. Live-born horse clones: claims 146, 153, 155, and 162 of the 233 application.

XIIb. Live-born horse clones: claims 152–154, 161, 163, and 170 of the 862 application.

The Examiner noted that the enablement of claims limited to live born clones of cattle, sheep, pigs, and goats was not challenged. (*Id.* at 6.)

The Examiner expressly considered the nature of the invention (Answers at 7), the value of the guidance provided by the specification, including the working example of cloning a sheep (*id.* at 9), and the state of the art at the time of filing as indicated by post-filing publications (*id.* at 7-8).

The Examiner describes the nature of the invention in terms that indicate that the art is sophisticated, complex, and that the success rate was low: the 233 application reports that one out of 78 somatic nuclear transfers developed to produce a live lamb (233 Answer at 9), while the 862 application reports that 277 "fused couplets" (oocytes with a transferred embryonic nucleus) resulted in a single live birth (862 Answer at 9).[19] The

[19]The Examiner's reference to "transferred embryos" (862 Answer at 9) may need clarification. The 862 Brief and the 862 Specification indicate 78 nuclear transfers into oocytes resulted in 10 embryos, which were then transferred to six ewes, of which one established a twin pregnancy, which resulted in the birth of a single live lamb (862 Brief at 12; 862 Specification at 28). According to the 862 Specification, the results shown in Tables 4 and 5 relate to the "development of ovine [sheep] embryos reconstructed by transfer of an embryo derived established cell line to unactivated enucleated *in* vivo matured ovine oocytes." (862 Specification at 27:6–8.)

The 233 Brief and the 233 Specification indicate that one live lamb resulted from 277 nuclear transfers (Table 4, OME (ovine mammary epithelial cell line derived from an adult 6-year old Fin-Dorset Ewe (233

Examiner found further that the disclosure of the embryonic nuclear transfer in the 862 application was minimally relevant to the claimed subject matter, which requires transfer of a somatic nucleus. (*Id.*) The Examiner also found that the somatic nuclear transfer process described for sheep in the 233 specification was not sufficient to guide successful somatic nuclear transfer cloning in rabbits, mice, rats, and horses. (233 Answer at 9.)

As evidence of the state of the art as of the 1995 filing date regarding the four challenged mammalian clones, and as evidence of the quality and quantity of experimentation that would have been required to make those claimed cloned mammals, the Examiner relied on the following references, all of which were published after the Campbell priority applications were filed in 1995:

Wakayama[20] (1998: mice);

Chesné[21] (2002: rabbits);

Fitchev[22] (1999: failure to clone rats) and Zhou[23] (2003: rats); and

Galli[24] (2003: horses).

Specification at 32:5–10).)

[20]T. Wakayama *et al.*, *Full-term Development of Mice from Enucleated Oocytes Injected with Cumulus Cell Nuclei*, 394 *Nature* 369-374 (1998) (*Letter to Nature*, 6 pages, 5 figures, 3 tables, separate Methods section).

[21]Patrick Chesné *et al.*, *Cloned Rabbits produced by nuclear transfer from adult somatic cells*, 20 *Nature Biotechnology* 366-369 (2002) (*Research Article*, 4 pages, 3 figures, 1 table, separate experimental protocol section).

[22]P. Fitchev *et al.*, *Nuclear Transfer in the Rat: Potential Access to the Germline*, 31 *Transplantation Proc.* 1525-1530 (1999).

[23]Qi Zhou *et al.*, *Generation of Fertile Cloned Rats by Regulating Oocyte Activation*, 302 *Science* 1179 (2003).

Based on these references, the Examiner found that at the time of filing in 1995, "the skilled artisan would have regarded the cloning of mice, rabbits, horses and rats to be unpredictable." (233 Answer at 7; 862 Answer at 8.)

Campbell responded that the Examiner had failed to properly account for the low efficiency of the disclosed process. (*E.g.*, Briefs at 12.) Campbell argued that because it would have been necessary only to repeat the disclosed process for each of the claimed species, the experimentation would have been routine, not undue. (*Id.* at 12–13.) Moreover, according to Campbell, the Examiner failed to present evidence that the recited and disclosed process would not succeed, if repeated often enough. (*Id.* at 13.) Campbell concluded that the Examiner had erred by mistaking improvements in efficiency of known processes for evidence of nonenablement. (*Id.* at 13–14 (mice), at 15–16 (rabbits), at 17–18 (horses), and at 19 (rats).)

More particularly, Campbell argues that the disclosure in its specification of a 6–20 hour interval between nuclear injection and oocyte activation for the cloning of cows would have suggested the 1-6 hour delay found by Wakayama to be critical for the cloning of mice. (Briefs at 13–14.) Similarly, Campbell argues that the asynchronous period or 22 hours found by Chesné to be critical would have been suggested by the work of Landa[25] on embryo transfer with in vitro cultured, previously frozen rabbit embryos,

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[24]Cesare Galli et al., *A Cloned Horse Born to its Dam Twin*, 424 *Nature* 635 (2003) (*Brief Communication.*)

[25]V. Landa, *Factors Influencing the Results of Transfers of Rabbit Embryos Stored at -196°C*, 27 *Folia Biologica (Praha [Prague])* 265-273 (1981).

and by the work of Al-Hasani[26]. (Briefs at 15–16.) As for the horse cloning, Campbell argues that the techniques taught by the references merely describe activation studies done with compounds known to be useful in oocyte activation protocols before Campbell's priority date. (Briefs at 17-18.) Campbell's arguments are not supported by a declaration from a skilled worker in the art.

In response to Campbell's criticisms, the Examiner cited the following additional references (Answers at 19-21):

Pennisi[27] (2000),

Polejaeva[28] (2000), and

Westhusin[29] (2001).

The Examiner argued that these reference show that the alleged "general low efficiency" was actually evidence that undue experimentation without a predictable degree of success would have been required to make and use the claimed inventions. (E.g., Answers at 20.)

We begin by considering the evidence of the state of the art (and the level of ordinary skill) presented in the general references.

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[26]S. Al-Hasani et al., *In vitro Fertilization and Embryo Transfer of Pre-ovulatory Rabbit Oocytes*, 21 *Eur. J. Obstet. Gynecol. Reprod. Biol.* 187-195 (1986).

[27]Elizabeth Pennisi and Gretchen Vogel, *Clones: A Hard Act to Follow*, 288 *Science* 1722-1727 (2000) ("News Focus" article).

[28]Irina A. Polejaeva *et al.*, *Cloned Pigs Produced by Nuclear Transfer from Adult Somatic Cells*, 407 *Nature* 86-90 (2000).

[29]M.E. Westhusin et al., *Cloning to Reproduce Desired Genotypes*, 55 *Theriogenology* 35-49 (2001).

Westhusin

Westhusin, published in 2001, summarizes the state of the art of mammalian cloning at that time. According to Westhusin, "[c]loning a particular animal in order to reproduce a specific genotype can be an extremely challenging venture. A number of different variables may affect the work effort required and the probability for producing a clone." (Westhusin at 36.) Westhusin continues:

> Without a doubt, one of the major factors influencing the probability of cloning a specific animal is species. While the basic approach involving nuclear transfer may be similar, the specific materials and methods utilized for cloning one species of animal do not automatically apply across different species. Cloning animals by nuclear transplantation involves several key steps including: 1) acquisition of mature ova, 2) removing the chromosomes contained within the ova (enucleation), 3) transfer of cell nuclei obtained from the animal to be cloned into enucleated ova, 4) activation of the newly formed embryo so as to initiate embryonic development, 5) embryo culture in vitro, and 6) transfer of the cloned embryo into a surrogate mother. Techniques that are required to accomplish each of these steps will vary slightly between species. More important, the efficiency of each step varies among species, ultimately affecting the ease of which a particular animal can be cloned.

(Westhusin at 36–37; emphasis added.)

Westhusin comments briefly on the successful cloning of cattle, sheep, goats, mice, and pigs, of which we need only quote the remarks on pigs emphasizing the variability among species:

> [a]s with mice the production of cloned pigs has been difficult and very inefficient with only around 1% of the embryos transferred surviving to term. Moreover, this figure does not represent the numerous trials that have resulted in no offspring. Pigs represent an excellent example for pointing out that

> assisted reproductive technologies and techniques for nuclear transfer don't directly apply from one species to another.

(Westhusin at 39; emphasis added.)

Westhusin also reports on its own unsuccessful attempts to clone dogs (*id.* at 40), before discussing the effects of nuclei donor cell types and the effects of genetic modifications. The paper closes with the comment, "[t]he ability to clone an animal of any given species will ultimately depend on the amount of research specifically focused on that species. With advancements in research, the ability to clone a specific animal will depend on perseverance." (*Id.* at 46; emphasis added.)

Pennisi

Pennisi, a "News Focus" article published in the journal *Science* in June 2000, presents an overview for a general technical audience of the state of the art in cloning mammals, based in part on reporting from a 'closed-door conference' held in the spring of 2000 at the Cold Spring Harbor Laboratory. (Pennisi at 1722:3.) The theme of the article, announced in the header, reads, "[d]espite scores of cloned animals, the process is fraught with problems. Many researchers are going back to the lab to find out why." (*Id.* at 1722.) The article continues, "[w]hat the press accounts often fail to convey is that behind every success lie hundreds of failures—some so daunting that many would-be cloners have put efforts to create live animals on hold and are going back to the lab to study why cloning sometimes works but far more often fails." (*Id.* at 1722:1.) Jean-Paul Renard[30], of the National Institute of Agricultural Research, in France, is quoted as saying

[30]Renard is the corresponding author of both Chesné (2002) and Zhou (2003), both of which are discussed *infra*.

about the state of cloning, "[w]e have no explanation; it's more art than science." According to Pennisi, Wilmut and Campbell—the present applicants—"spent years painstakingly manipulating both the donor cells and the receiving eggs, developing the finesse to make nuclear transfer work with differentiated cells." (*Id.* at 1723:1.) Pennisi characterizes their eventual successful experiment (Dolly, a cloned sheep) as "paradigm-altering." (*Id.*)

Pennisi summarizes the state of the art for several species. Cattle, perhaps the most successfully cloned mammal, appeared in 2000 to remain somewhat problematic due to developmental abnormalities arising from unresolved sources in a significant number of cloned offspring. "Cloning veteran Jim Robl of the University of Massachusetts" (Pennisi at 1722:2) is quoted as saying, "[w]hat we still have is a black box" (*id.* at 1724:3).

Regarding pigs, Pennisi relates that [Randall] Prather[31], "[a]fter almost three frustrating years of trying to clone pigs [by SCNT] . . . was close to calling that goal unachievable. Hiroshi Nagashima of Meiji University in Tokyo . . . had a similar tale of woe." (*Id.* at 1724:3 to 1725:1.) Pennisi relates the success of a third group, PPL Therapeutics[32], in the following words:

> Ayares says PPL spent more than a year trying to clone pigs with the techniques the company and Wilmut had used for sheep. Each attempt failed. . . . Then 2 years ago, company scientists junked that approach and hit upon an entirely new—and apparently successful—one that Ayares will not discuss

[31]Prather is the lead author of Prather (1989), cited *supra*, which describes the cloning of pigs using pig embryonic cells as nucleus donors.

[32]The work of this group appears to be that reported by Polejaeva, discussed *infra*.

> until the scientific paper comes out—other than to say that he is confident that PPL can clone more pigs when they want to. . . . Prather, however, is witholding judgment until he sees more piglets. "I think they got lucky," he says of PPL.

(*Id.* at 1725:1–2; emphasis added.)

Pennisi indicates that species differences are highlighted by goats and rabbits. "Goats, it seems, are easy." (Pennisi at 1725:2.) "On the other hand, despite their natural fecundity, rabbits have so far defied efforts to produce them in the lab. 'We can get a lot of cloned embryos,' says Renard . . . 'but all pregnancies abort after transfer to a surrogate mother.'" (*Id.* at 1725:2.)

Finally, Pennisi discusses the successful cloning of mice by Teruhiko Wakayama[33], in 1998. (Pennisi at 1727:2.) "Even in Wakayama's skilled—and some say 'magic'—hands, cloning is unpredictable and enigmatic." (*Id.*) Following a move from Honolulu to Rockefeller University, Wakayama reportedly could not reproduce his successful cloning of mice for some time. Moreover, "other labs remained frustrated in their efforts to duplicate Wakayama's work, prompting some disbelief." (*Id.*) Eventually, however, other groups managed reproduce Wakayama's success. (*Id.* at 1727:2–3.)

Polejaeva

Polejaeva, published in the journal *Nature* in September 2000, appears to be the formal report of the break-through described by Pennisi for SCNT-cloned pigs noted *supra*. Ayares, noted *supra*, and Campbell, one of the present applicants, are among the co-authors. Polejaeva remarks that "[a] variety of factors probably contribute to this inefficiency [1–2% efficiency

[33]This work is reported in Wakayama (1998), discussed *infra*.

of somatic cell nuclear transfer, as measured by development to term, *i.e.*, live birth]:

> These include laboratory to laboratory variation, oocyte source and quality, methods of embryo culture which are more advanced in some species (such as cows) than others (such as pigs), donor cell type, possible loss of somatic imprinting in the nuclei of the reconstructed embryo, failure to reprogram the transplanted nucleus adequately, and finally, the failure of artificial methods of activation to emulate reproducibly those crucial membrane-mediated events that accompany fertilization.

(Polejaeva at 86:2.) Polejaeva goes on to say, "[w]e cannot currently address all of the methodological problems, and, to improve our chances of success in pig nuclear transfer, we chose to focus on four areas: activation, choice of donor cell, embryo culture, and induction and maintenance of pregnancy." (*Id.* at 86:2–87:1.)

Polejaeva summarizes their successful cloning of pigs from differentiated (somatic) pig cells in the following words:

> We think that the principal reasons for the success of this modified nuclear transfer procedure in pigs is its lack of reliance on current artificial activation protocols and *in vitro* culture techniques. Although elaborate, the double nuclear transfer does not add another major inefficiency (the second step fusion is very efficient). Direct transfer of a somatic nucleus to an enucleated zygote will not work because (in addition to reprogramming difficulties) of the loss of important factors sequestered within the removed pronuclei. The cell population used successfully as nuclear donors in these experiments were not quiesced by serum starvation. . . . [certain test results suggest] that most cells in the population were in the G1 phase of the cell cycle and not arrested in G0.

(*Id.* at 89:1; emphasis added.)

We find it interesting that the 233 specification describes, and claims 146–154 of the 233 application require, that "the somatic cell or cell obtained by culture thereof [the nuclear donor cell] is in a quiescent diploid cell at the time of transfer." (Brief Claims App. at 1; 233 specification at 5:5-8.) In contrast, however, the 862 specification describes, and claims 152–162 of the 862 application require, that "the differentiated cell or cell obtained by culture thereof [i.e., the nuclear donor cell] is a diploid cell in the G1 phase of the cell cycle at the time of transfer." (862 Brief Claims App. at 1; 862 specification at 4:1-4.)

Species References

Wakayama (1998, mice)

Wakayama reports injecting nuclei from three different somatic cell types into enucleated mouse oocytes in the G0 phase of the cell cycle. (Wakayama at 369–370.) A delay of 1 to 6 hours between nucleus injection and oocyte activation appeared to provide a significant improvement in development to morulae/blastocysts, but nuclei from cumulus cells (cells that surround developing egg cells) provided significantly higher yields than nuclei from sertoli cells (associated with developing sperm cells) or neuronal (brain) cells. (*Id.* at 370–71; Tables 1 and 2.) Wakayama reports that six live fetuses were obtained from 298 embryos transferred to 18 foster mothers, and that Cumulina, the first surviving cloned mouse, produced pups following mating with a normal mouse. (*Id.*, see also Figure 2, showing photographs of the mouse clones.) Moreover, clones of the clones were also obtained: 287 embryos derived from cumulus-cell nuclei were

then transferred to 18 foster mothers, from which eight live fetuses were recovered. (*Id.*)

According to Wakayama, the previous practice was to activate the renucleated oocytes immediately after injection. Delays of 30 to 60 minutes are said to have resulted in abnormalities, with none of the embryos developing beyond the 4-cell stage. (Wakayama at 372:2, first full paragraph.) In Wakayama's words, "[a]lthough this [the prolonged interval between nuclear injection and oocyte activation] seems paradoxical after earlier work, prolonged exposure of incoming nuclei to a cytoplasm rich in metaphase promoting factor causes persistent chromosome condensation (in the absence of DNA synthesis) and may facilitate the nuclear changes that are essential for development." (*Id.* at 373:1; emphasis added.) Wakayama also proposes that finding that sertoli and neuronal cell nuclei failed to produce full term embryos "suggests that the G0 status of donor nuclei is not sufficient *per se* to ensure embryonic development. . . . several regulatory morphogenic factors and checkpoints may be involved in the development of post implantation embryos/fetuses." (*Id.*; emphasis added.)

Chesné (2002, rabbits)

Chesné, a "Research Article" in the journal *Nature Biotechnology*, was published in April 2002[34], about seven years after the 1995 priority date of Campbell, and two years after the Cold Harbor conference described by Pennisi. Chesné describes the first successful cloning of rabbits by nuclear transfer from adult somatic cells. According to Chesné, success was gained only after extending the asynchrony between donor and recipient females

[34]The receipt date is said to have been 18 October 2001. (Chesné at 368.)

from 16h (complete failure of pregnancy) to 22h (1.6% of transferred embryos resulted in kits born). Chesné notes that "[s]uch a marked asynchrony at early cleavage stages of development had not been attempted previously with NT embryos, but can be compatible with full-term development of fertilized eggs." (Chesné at 367:1.) Chesné concludes that its results "show that the former limitations to successful rabbit somatic cloning have been overcome by taking into account species differences in oocyte physiology and early embryonic development." (*Id.* at 367:2.)

Fitchev (1999, failed rats)

Fitchev, published about four years after Campbell's priority date, cites previous work on cloning sheep and cattle from embryonic fibroblast nuclei, rabbits and primates from embryonic stem cells or blastomeres, and mice from adult cumulus cells [Wakayama, supra], and reports "preliminary evidence on the several steps necessary to develop rats from the nuclei of cultured cells." (Fitchev at 1526:1.) According to Fitchev, they were able to reconstitute rat embryos from cultured embryonic fibroblast nuclei injected into enucleated metaphase II oocytes by cell fusion followed by activation with DC pulses of electricity. (*Id.* at 1526:1–1527:2.) In Fitchev's words, "[t]he reconstituted embryos were placed in the reproductive tract of surrogate mothers for further development but at this time none have been successfully recovered (Table 3)." (*Id.* at 1528:1; emphasis added.) Although Fitchev expresses optimism, several areas of further research are identified, including methods of fusion and activation (*id.* at 1528:1 to 1529:1), and whether there is significant species-variation of the effect of the cell cycle that affects the reprogramming of the nucleus for development (*id.* at 1529:1–2). Moreover, Fitchev states that culture from the one-cell

stage to the blastocyst stage "has been particularly frustrating in the rat." (*Id.* at 1529:2.) Fitchev concludes that "[c]learly much work needs to be done to make routine production of rats from nuclear transfer a reality, but many interesting scientific outcomes can be expected along the way." (*Id.*; emphasis added.)

Zhou (2003, rats)

Zhou, in a one-page "Brevia" published in the journal *Science* in 2003, some eight years after Campbell's 1995 priority date, describes the first successful cloning of rats via SCNT cloning. Fibroblast (muscle cell) nuclei were micro-injected into enucleated oocytes. In addition to a one-step rapid procedure initially developed to address the rapid activation of rat oocytes following removal from the oviducts, Zhou used MG132, a protease inhibitor that Zhou determined reversibly stabilized most oocytes in metaphase II for up to 3 hours. From 876 implanted embryos implanted into 12 prepared foster rat females, four of the females were found to contain 16 fetuses. In a subsequent experiment, 129 cloned embryos were transplanted into two foster mothers. One of the foster mothers contained fetuses, and she delivered 3 live male pups, one of which died within hours of birth. The other two survived to sexual maturity and generated normal progeny.

Galli (2003, horses)

Galli describes, in a Brief Communication of less than one page in the journal *Nature*, in 2003, the birth of a live foal, one of four pregnancies developed from a total of 22 blastocysts developed (8 from 513 male and 14 of 328 female cell line embryos reconstructed by fusion of fibroblasts

with oocytes). According to Galli, "[t]his success was aided by advances in assisted reproduction in the horse, particularly at the oocyte activation stage, when protein synthesis and phosphorylation must both be inhibited, and in the refinement of the zona-free manipulation technique." (Galli at 635:2; four citations, two published in 2002 and two published in 2003, omitted.)

Enablement: Discussion

We have no difficulty concluding from Campbell's disclosures and from the art summarized *supra* that the nature of the invention is highly sophisticated, involving the confluence of many fields of research and technology ranging from molecular biology to animal husbandry. The level of ordinary skill is correspondingly high: ordinary workers in the relevant arts are capable of performing complex tasks and solving complex problems in a variety of disciplines. We also find that the art was (and remains) rapidly advancing, and that the inventors were (and remain) at the forefront of the field.

We also have no difficulty concluding that the art of somatic cell nuclear transfer cloning remains highly unpredictable in 2007, and that it was much more so in 1995. Inter-species variation has been identified as a major obstacle (Pennisi, Westhusin, Polejaeva) to progress. There can be no doubt that interspecies variation was also a major concern in 1995. The record indicates that it was necessary to conduct fundamental research on each of the four challenged species before it was possible to carry out the general program of somatic cell nuclear transfer cloning successfully to term. It appears that prominent and respected scientists strove mightily to advance the field and failed repeatedly for a long time, particularly with the

species identified by the Examiner as lacking an enabling disclosure. Wakayama's report of successful cloning of mice in 1998 met with respectful skepticism three years after Campbell's priority date because it could not be reproduced by others. In 1999, Fitchev reported on their failure to clone rats a year after Wakayama reported the successful somatic transfer cloning of mice. In 2000, Renard could only report failed pregnancies in attempts to clone rabbits by somatic transfer. Prather was reportedly on the verge, in 2000, of calling pig cloning by SCNT impossible; Nagashima too had failed to clone pigs in that manner. After two years of effort, PPL (Polejaeva, Ayares, Campbell, and others) are said to have "junked" the approach Wilmut and Campbell had used for sheep. The junked approach appears to have been similar to the procedures described in the 233 and 862 applications. In its place, they developed a technique that they would not reveal in March 2000, at the Cold Spring Harbor meeting of the top workers in the art. They reported the successful SCNT cloning of pigs later that year in the leading journal *Nature*.

It is also apparent that within each of the challenged species, specific problems had to be identified and overcome, often by taking a new route. Mice, for example, were not successfully cloned until Wakayama resorted to delaying activation of the renucleated oocytes—a procedure that had previously been identified as resulting in abnormalities that prevented embryos from developing past the four-cell stage. This step, according to Wakayama, "seems paradoxical after earlier work." Taking a "paradoxical" step is not characteristic of routine experimentation; rather, it is strong evidence that the nature of the required experimentation was original research and not obvious to the person having ordinary skill in the art. *Cf.*

In re Hedges, 783 F.2d 1038, 1041 (Fed. Cir. 1986) ("proceeding contrary to the accepted wisdom . . . is strong evidence of unobviousness.") (internal quote and citation omitted). Indeed, others had so much trouble reproducing that work that there was "some disbelief." Wakayama was reportedly viewed as having "magic hands." It apparently took the better part of two years before others were able to begin to reproduce the technique. These facts also tend to support the conclusion that the amount and nature of experimentation required in 1995 would have been undue.

The successful cloning of rabbits was achieved only after trying a "marked asynchrony" that had not previously been tried with nuclear transfer embryos. The report did not appear until two years after Renard had apparently reported failure at the Cold Spring Harbor conference in 2000. The nature of the failed efforts and of the eventual success appear to be characteristic of original research in an area where there are few if any reliable explanations. We find that they support the Examiner's conclusion that undue experimentation would have been required to clone rabbits by somatic nuclear transfer in 1995.

The successful cloning of rats followed at least a double discovery—the development of a one-step procedure designed to address the too-rapid activation of rat oocytes following removal from the oviducts, and the use of a protease inhibitor that was determined to stabilize "most oocytes" at a particular stage (metaphase II). Campbell has not indicated where these particular problems and the eventual solution were identified, either in the prior art or in its specifications. Again, the weight of the evidence suggests that these discoveries were the result of original research, not mere optimization of known procedures.

Similarly, the report of successful cloning in horses cites four publications, two in 2002 and two in 2003, as having "aided" the successful cloning by somatic cell nuclear transfer. In the absence of some detailed explanation, we find it unlikely that, seven or eight years earlier, a person of ordinary skill in the art would have been able, based on the knowledge in the prior art and in Campbell's specifications, without the advances reported in the publications of 2002 and 2003, to clone a horse without undue experimentation.

Campbell's arguments that the subsequent papers merely improved the efficiency of known processes are not persuasive. The argument with respect to mice is belied by Wakayama's statements that the steps taken "seems paradoxical after earlier work" (Wakayama at 373:1). This statement, made in a leading journal, was subject to critical review by experts in the field. Peer review is not a guarantee of the accuracy of the papers that pass scrutiny, but we do not find it credible that such a statement in an important Letter to *Nature* would have passed unchallenged. Accordingly, we find Wakayama's statements more credible than Campbell's, which were made in the course of seeking to obtain exclusionary patent rights. Moreover, if the new steps were routine optimizations, why did it take so many failures to adopt them—and if they were routine, why did it take what seems like original research to develop them?

Campbell has not directed our attention to evidence that even the highly skilled leaders in the art would have recognized, in the teachings of Campbell's 1995 disclosures, alone or in combination with what was known in the art, the problems that needed optimization and the means of

optimization. We find the disclosures in Campbell's specifications to be very general compared to the disclosures of the eventual successful SCNT cloning of the challenged species, namely mice, rats, rabbits, and horses (taking into account the four post-2002 publications on assisted reproduction of horses said to have aided the success). The general disclosure of a large set of techniques, some of which are generic to an eventually successful set of procedures, is not necessarily equivalent to an enabling disclosure. The amount of difficulty encountered in achieving SCNT cloning in the challenged species is highlighted in this record by Westhusin's statement that "[t]he ability to clone an animal of any given species will ultimately depend on the amount of research specifically focused on that species. With advancements in research, the ability to clone a specific animal will depend on perseverance." (Westhusin at 46.) If research needs to be focused specifically on a given species, and if advancements in research are needed to attain the ability to clone species by perseverance, the effort required to clone that species is unlikely to be routine.

The art cited by Campbell is not persuasive. Although both Landa[35] and Al-Hasani[36] are concerned with improving the transplantation of rabbit embryos, there is no indication that these papers have ever been recognized by those skilled in the relevant arts as providing valuable teachings that would have been useful for solving the problems encountered by those seeking to clone rabbits. The record indicates the contrary. For example,

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[35] V. Landa, *Factors Influencing the Results of Transfers of Rabbit Embryos Stored at -196° C*, 27 *Folia Biologica (Praha)* 265–273 (1981).

[36] S. Al-Hasani *et al.*, *In Vitro Fertilization and Embryo Transfer of Pre-ovulatory Rabbit Oocytes*, 21 *Eur. J. Obstet. Genecol. Reprod. Biol.* 187–195 (1986).

Renard, in 2000, apparently had not identified synchronicity as a critical factor that needed to be optimized, despite his groups involvement with rabbit cloning. We conclude that the weight of the evidence shows that the "optimizations" necessary to obtain SCNT cloned rabbits were not routine.

Similarly, Campbell's arguments that the "advances" said by Galli to have aided the SCNT cloning of a horse were simply optimizations of what was already known are not persuasive. In this case, the passage of time between the report of successful sheep cloning (Dolly) and the first report of a successful SCNT cloning of such a common animal as a horse suggests that there were many difficulties that had to be overcome along the way. That certain issues were known to be problems, and that the eventual solutions to those problems were also known in another context does not establish that the effort required to bring the potential solution together with the problem at hand was "mere optimization." Again, we find that Galli's statements that advances by others were prerequisites to his group's eventual success support the conclusion that the amount of effort required to successfully clone a horse, based on Campbell's disclosure and what was already known in the art would have been undue in 1995.

Far from simply repeating the procedures taught by Campbell in the 1995 priority document, success in each of the challenged species followed years of failure, and efforts to learn what fundamental properties of the development of each species were causing the simpler methods to fail. The turn by some researchers—Wilmut reportedly among them—away from cloning per se to more fundamental problems, such as how genes in somatic nuclei are reprogrammed in the cloning process (Pennisi at 1722:1), and the discouragement of others, such as Prather, run strongly counter to

Campbell's protestations that all that was necessary was to continue to turn the crank, to repeat what had succeeded in sheep, to "optimize" conditions for other animals. Before characterizing a new procedure as an "optimization," it is fair to demand a reasonable expectation of successfully obtaining the underlying goal. "Improving failure" is an oxymoron. As the Federal Circuit has noted, "[w]here, as here, the claimed invention is the application of an unpredictable technology in the early stages of development, an enabling description in the specification must provide those skilled in the art with a specific and useful teaching." *Genentech Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1367-68 (Fed. Cir. 1997). "Tossing out the mere germ of an idea does not constitute enabling disclosure." *Id.* at 1366. The record indicates that the Examiner has accepted, in effect, such a characterization for sheep, cattle, goats, and even pigs. We conclude that the record strongly supports the Examiner's contrary conclusion that no such reasonable expectation of success existed for rabbits, mice, rats, and horses. The record shows that the nature of research required was, in the end, far beyond routine optimization.

Campbell's argument that the Examiner erred by failing to prove that the disclosed processes would not succeed, eventually, by continued repetition, has no basis in law. The concept of "undue experimentation" is founded on the practical realities of the research laboratory or the industrial workplace. The right to exclude all others from making or using the claimed subject matter is granted in exchange for the teachings of how to make and use it. Thus, a procedure must be reproducible in a meaningful period of time. In the scientific research world—and much more so in the "real world" of commerce and medical therapy—great difficulties of reproducing

results lead—as they did for Wakayama's mouse-cloning techniques—to doubt that a useful procedure has been described. Reproducibility on a time-scale deemed relevant by those skilled in the art is a measure of undue experimentation. The inability to obtain or to reproduce a result in a reasonable period of time with a reasonable amount of effort is indistinguishable from the inability to make and use the invention. The failure of leading workers in the art to clone rabbits, mice, rats, and horses until they made substantial advances in research weigh more heavily than Campbell's arguments that all that was needed was more trials.

An additional indication of the non-routine nature of the necessary efforts come from the timing and the places of the publications. The *Nature* journals, and *Science*, are particularly "high profile" publications that seek, as *Nature* puts it, to publish "the finest peer-reviewed research in all fields of science and technology on the basis of its originality, importance, interdisciplinary interest, timeliness, accessibility, elegance and surprising conclusions. *Nature* also provides rapid, authoritative, insightful and arresting news and interpretation of topical and coming trends affecting science, scientists and the wider public."[37] According to *Nature*, its main formats for original research are Articles and Letters.[38] Articles are said to be "original reports whose conclusions represent a substantial advance in understanding of an important problem and have immediate, far-reaching implications." (*Id.*) Letters are said to be "short reports of original research focused on an outstanding finding whose importance means that it will be of interest to scientists in other fields." (*Id.*) *Science* has similar standards,

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[37]http://www.nature.com/nature/about/index.html.

[38]http://www.nature.com/nature/authors/gta/index.html.

characterizing "Brevia" as short works that "present research results on subject matter attractive to, and understandable by, scientists from a wide a wide range of fields. Interdisciplinary work, or experiments or analyses that produce a result of general interest, are especially appropriate for this section. Authors should avoid highly technical presentations and jargon specific to particular disciplines." All of the articles cited by the Examiner, with the exception of Pennisi, are reports of original research that were subjected to peer review.

As the Federal Circuit remarked, discussing the impact of articles published in prestigious journals:

> Calgene suggests that if the successes set forth in these articles, especially those successes in eukaryotes, were mere routine experimentation based on the written descriptions in the patent specifications, it is unlikely that they would have been published in such prestigious journals. *See e.g.*, Preface to the journal *Cell*, J.A. at A26,984 ("Cell publishes reports of research of exceptional significance in any area of biology. Papers will not be considered for publication only if they report novel results of interest to a wide audience."). We agree with Calgene that citation of these articles in the declaration is as much a suggestion of nonenablement as enablement.

Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1376 (Fed. Cir. 1999).

The rejection of claims to rabbits, mice, rats, and horses for lack of an enabling disclosure is AFFIRMED.

C. Summary (233 Application)

In view of the record and the foregoing considerations, it is:

ORDERED that the rejection of claims 146-163 of the 233 application under 35 U.S.C. § 101 as being drawn to non-statutory subject matter is AFFIRMED;

FURTHER ORDERED that the AFFIRMANCE of the rejection of claims 146-163 of the 233 application under 35 U.S.C. § 101 is entered as a NEW GROUND OF REJECTION;

FURTHER ORDERED that the rejection of claims 146-163 of the 233 application over claims 152–171 of the 862 application as being drawn to the same statutory invention is AFFIRMED;

FURTHER ORDERED that the rejection of claims 146, 147, 155, and 156 of the 233 application (clones of cattle) under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Sims is AFFIRMED;

FURTHER ORDERED that the rejection of claims 146, 148, 155, and 157 of the 233 application (clones of sheep) under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of McLaughlin is AFFIRMED;

FURTHER ORDERED that the rejection of claims 146, 149, 155, and 158 of the 233 application (clones of pigs) under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Prather is AFFIRMED;

FURTHER ORDERED that the rejection of claims 146, 150, 155, and 159 of the 233 application (clones of goats) under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Yong is AFFIRMED;

FURTHER ORDERED that the rejection of claims 146, 151, 155, and 160 of the 233 application (clones of mice) under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Cheong is AFFIRMED;

FURTHER ORDERED that the rejection of claims 146, 152, 155, and 161 of the 233 application (clones of rabbits) under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Yang is AFFIRMED;

FURTHER ORDERED that the rejection of claims 146, 153, 155, and 162 of the 233 application (clones of horses) under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Lawrence is REVERSED;

FURTHER ORDERED that the rejection of claims 146, 154, 155, and 163 of the 233 application (clones of rats) under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103(a) in view of Gonzales-Pacheco is REVERSED;

FURTHER ORDERED that the rejection of claims 146, 151-155, and 160–163 of the 233 application for lack of an enabling disclosure under 35 U.S.C. § 112(1) is AFFIRMED;

FURTHER ORDERED that our decision is not a final agency action.

FURTHER ORDERED that within **two (2) months** from the date of our decision appellant may further prosecute the application on appeal by exercise one of the two following options:

1. Request that prosecution be reopened by submitting an amendment or evidence or both. 37 C.F.R. § 41.50(b)(1) (2006).

2. Request rehearing on the record presently before the Board. 37 C.F.R. § 41.50(b)(2) (2006).

FURTHER ORDERED that any request for rehearing on the present record shall be EXPEDITED.

FURTHER ORDERED that no time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv) (2006).

AFFIRMED
(New rejection under Bd. R. 41.50(b))

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